



# UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
United States Patent and Trademark Office  
Address: COMMISSIONER FOR PATENTS  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 10/717,101      | 11/19/2003  | Harold L. Atkins     | 18013-C1            | 7313             |

31976 7590 04/21/2006

LEWIS J. KREISLER  
LEGAL DEPARTMENT  
930 CLOPPER ROAD  
GAITHERSBURG, MD 20878

EXAMINER

LI, BAO Q

ART UNIT PAPER NUMBER

1648

DATE MAILED: 04/21/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

10/717,101

Applicant(s)

ATKINS ET AL.

Examiner

Bao Qun Li

Art Unit

1648

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 02 February 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1,3-5 and 10-24 is/are pending in the application.
- 4a) Of the above claim(s) 10-16 and 18 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,3-5, 17, 19-24 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>07/25/05&amp;09/28/05</u> | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

Claims 1, 3-5, 10-24 are pending before the examiner.

#### ***Response to Amendment***

This is a response to the amendment filed on 02/02/06. Claims 1, 22 and 24 have been amended. Claims 2 and 6-9 have been canceled. Claims 10-16 and 18 have been withdrawn from consideration. Claims 1, 3-5, 17, 19-24 are considered before the examiner.

Please note any ground of rejection(s) that has not been repeated is removed. Text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

#### ***Information Disclosure Statement***

1. The information disclosure statement (IDS) submitted on September 27, 2005 was filed after the mailing date of the previous office action on September 30, 2005. The submission is in compliance with the provisions of 37 CFR 1.97. The IDS that was not considered and signed in the previous office action was due to the cross-mail. Accordingly, the information disclosure statement is being considered by the examiner in the office action.

#### ***Double Patenting***

1. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

2. An obvious-type double patenting rejection is appropriate where the conflict claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g. Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

3. Claims 1 is still provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable distinct over claim 35 of copending Application No. 09/664,444 in view of Weber et al. (Crit. Rev. Eukaryot Gene Expr. 2000, Vol. 10, No. 3-4, pp. 281-302) and Rummel et al. (J. Hematotherapy 1994, Vo. 3, pp. 213-218).

4. Claim 1 is still provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable distinct over claim 18 of copending Application No. 10, 743, 639 in view of Weber et al. (Crit. Rev. Eukaryot Gene Expr. 2000, Vol. 10, No. 3-4, pp. 281-302) and Rummel et al. (J. Hematotherapy 1994, Vo. 3, pp. 213-218). Because applicants did not raise objection about the rejection, the rejection is maintained.

5. For the above rejections, applicants did not either object about the rejections or assert any error for the ground of the rejection. Moreover, Applicants admit that they will file a terminal disclaimer if an allowable subject matter is indicated in the future prosecution. The rejections are therefore, maintained.

#### **New ground of rejections.**

##### ***Double Patenting***

6. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686

Art Unit: 1648

F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

An obvious-type double patenting rejection is appropriate where the conflict claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g. *Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (fed. Cir. 1985).

7. Claim 1 is still provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable distinct over claim 17 of copending Application No. 10,743,649 in view of *Weber et al.* (Crit. Rev. Eukaryot Gene Expr. 2000, Vol. 10, No. 3-4, pp. 281-302) and *Rummel et al.* (J. Hematotherapy 1994, Vo. 3, pp. 213-218).

8. Claim 1 of current application is drawn to an ex vivo method for reducing or eliminating neoplastic cells in a mixture comprising normal hematopoietic cells and neoplastic cells. The method comprises contacting said mixture with the VSV. Claim 17 of application 10,743,649 is drawn to a method for reducing the viability of a tumor cell within a population of tumor cells and non-tumor cells comprising administering VSV to the population of cells, wherein the VSV is an attenuated strain VSV and the tumor cells are melanoma cells.

9. Claim 17 of copending application is directed to use a species of VSV, i.e. an attenuated VSV, for treating a species of tumor cells, whereas claim 1 of current application is directed to use a generic VSV for treating all tumor cells. The scopes of conflict claims are overlapping since the attenuated VSV and melanoma cells are still belonged to one of scope of the generic VSV and a tumor cell. To this context, the species of claim 17 anticipates the claim 1.

Art Unit: 1648

10. While the reference claim 17 is directed to use a generic non-tumor cell, and the rejected claim 1 is drawn to a species of normal hematopoietic cells in particular. However, it is well known in the art that purging tumor cells ex vivo can only be done with hematopoietic stem cells in cancer autologous transplantation therapy because the major source for the non-tumor cells that are able to differentiate to other lineage of cells are hematopoietic stem cells in the autologous transplantation therapy, which may be contaminated with a little bit of other normal hematopoietic cell lineages. No other cell in the body has such differentiation ability, and is used for the autologous transplantation in cancer therapy. Secondly, most cancer is metastasized through the blood circulatory system to bone, which is the bank of hematopoietic stem cells as evidenced by Weber et al. (See abstract). Consequently, the great concern in the autologous hematopoietic stem cell transplantation is the contamination of the grafting cells with metastatic cancer cells as evidenced by Rummel et al. (J. Hematotherapy 1994, Vol. 3, pp. 213-218, see abstract). Therefore, a person with ordinary skill in the art in order to get the best result of purging the contaminated engrafting cells ex vivo would have been obviously to purge the hematopoietic cells with VSV rather than any other normal cell population. Hence, the claimed invention is a best and an obvious choice over the generically claimed normal non-tumor cells in the reference claim.

11. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

### *Claim Rejections - 35 USC § 112*

12. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claims 1, 3, 4, 5, 17, 19, 20, 21, 22 and 24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for an ex vivo method of using an effective amount of oncolytic vesicular stomatitis virus (VSV) at 0.00001 or 10 pfu per cell to purge a bone marrow or peripheral blood stem cell for an effective length of time that is

Art Unit: 1648

used for transplantation in cancer treatment, does not reasonably provide enablement for purging such transplanted cells by just contacting a VSV in any concentration for any length of time.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

14. The test of an enablement or scope of enablement is whether one skilled in the art could make and use the claimed invention from the disclosure in the application coupled with information known in the art would render undue experimentation (See *United States v. Theketrone Inc.*, 8USPQ2d 1217 (fed Cir. 1988)). Whether undue experimentation is required is not based upon a single factor but rather a conclusion reached by weighting many factors. These factors were outlined in *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and again in *re Wands*, 8USPQ2d 1400 (Fed. Cir. 1988), which are set forth below: 1). Nature of invention; 2). Scope of claims; 3). State of art; 4). Unpredictability; 5). Level of skill; 6). Number of working examples and 7). Amount of guidance presented in the specification.

15. The nature of invention is directed to an ex vivo method of using an effective amount oncolytic VSV to purge bone marrow or peripheral blood cells that are harvested from a cancer patient and used for autologous transplantation after purging the possible contaminated cancer cell. The scope of the claims read on just contacting a VSV with a mixture of such suspension of transplanting cell.

16. The specification teaches an example of using VSV India serotype at the concentration of 0.05 pfu/cell or 0.0003 pfu/cell to selectively kill the leukemia cells when the leukemia cell line is co-cultivated with a normal cell line for 24 hrs or 48 hrs. While specification teaches that the oncolytic virus used for eliminating the undesirable cells is dependent on a virus selected. The specification does not teach that any concentration of VSV is able to selectively kill any undesirable cell by just a contacting. The specification fails to provide a sufficient evidence to support the broad scope of claimed invention.

17. It is well known in the art that any effective treatment of a disease requires to administration of a therapeutic agent in an effective amount for a effective period. Therefore, either a very large amount or a small amount of a therapeutic agent is not able to get a therapeutic effect. Especially for the biological active drug, such as a cytokine or a virus, it will

Art Unit: 1648

always produce some unexpected side effects. For example, Interferon gama-1b, though it is used in the clinic, it produces some adverse effect. If it is not administrated at a optimal dosage and a optimal period of time. If a severe side effect occurs, the dosage should be modified or the treatment should be interrupted until the adverse reaction abates (See Physician reference desk electronic library published on line entire page 1-10, especially page 3-7).

18. Given the above analysis of the factors which the courts have determined are critical in asserting whether a claimed invention is enabled, it must be considered that the skilled artisan would have to conduct undue and excessive experimentation in order to practice the claimed invention.

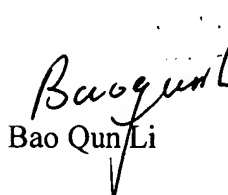
### *Conclusion*

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao Qun Li whose telephone number is 571-272-0904. The examiner can normally be reached on 7:00 am to 3:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

  
Bao Qun Li  
**BAOQUN LI, MD**  
**PATENT EXAMINER**

04/11/2006